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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,179	07/02/2003	Roland Kreutzer	14174-104USS/RIB001.3USD4	5239
26161	7590	08/07/2006	EXAMINER	
FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			VIVLEMORE, TRACY ANN	
			ART UNIT	PAPER NUMBER
			1635	
DATE MAILED: 08/07/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/612,179	Applicant(s) KREUTZER ET AL.	
	Examiner Tracy Vivlemore	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection or objection not reiterated in this Action is withdrawn.

Information Disclosure Statement

The information disclosure statement filed July 14, 2006 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. Therefore, the information in foreign patent documents DE 196 18 797 and EP 1 214 945 has not been considered. The information in references A19, A21 and A34 has been considered only to the extent of applicant's explanation of relevance.

Response to arguments: Claim Rejections - 35 USC § 102

Claims 4 and 6-9 remain rejected under 35 U.S.C. 102(b) as being anticipated by Crooke for the reasons set forth in the office action mailed January 25, 2006.

Applicant traverses the rejection over Crooke by stating that the dsRNA disclosed by Crooke would not specifically inhibit gene expression due to the presence of extensive 2'-O-methyl and phosphorothioate modifications. To support this assertion, applicant points to statements in Amarzguioui that "the most extensively

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phosphorothioate siRNA proved to be cytotoxic" and "It has been reported that siRNA with a general 2'-O-methylation in either strand have no activity." With regard to phosphorothioates, while it might be true that the phosphorothioate siRNAs studied by Amarzguioui produce a cytotoxic side effect, this is not evidence that siRNAs containing phosphorothioates are not active to inhibit gene expression. In fact, the art demonstrates exactly the opposite. In a recent review, de Fougères et al. (Methods in Enzymology 2005, vol. 392) teach that fully phosphorothioate siRNAs are active. The quote regarding 2-O-methyl substitution of siRNAs relied upon by applicant to demonstrate the dsRNA of Crooke et al. would be inactive appears to have been taken out of context. This sentence refers to the teachings of other references, however the teachings of Amarzguioui show that siRNAs containing 2'-O-methyl substitutions are active and in the sentence bridging pages 589-590 state that, "The 2'-O-methylation modifications, on the other hand, showed promise as they resulted in increased persistence of activity with no toxicity to cells."

Applicant also points to the reference of Kraynack and Baker to support their assertion that the dsRNA of Crooke would be inactive in inhibiting gene expression. This reference, however, describes siRNAs having complete substitution of the antisense strand with 2-O-methyl as inactive. The dsRNAs of Crooke, however, are not fully substituted and other skilled artisans (see for example, Prakash et al., J. Med. Chem. 2005) have found that partial substitution with 2'-O-methyl, even in the antisense strand, results in active siRNAs.

Claims 4-6 and 8 remain rejected under 35 U.S.C. 102(e) as being anticipated by Fire et al., as evidenced by Zhang et al. for the reasons set forth in the office action mailed January 25, 2006.

Applicant traverses the rejection over Fire as evidenced by Zhang by stating that the dsRNAs of Fire are all greater than 21 base pairs and Fire does not teach an "isolated" dsRNA of 15-21 base pairs. Applicant further argues that any isolated dsRNA taught by Fire is longer than the claimed range and therefore the action by Dicer occurs within a cell to non-isolated molecules. Applicant states that the reference of Zhang also describes action by Dicer within a cell. Applicant's arguments regarding the Fire and Zhang references are not persuasive because it is recognized that when the term "isolated" appears in a patent claim, it is meant to differentiate compounds that involve the "hand of man" from compounds that are products of nature. The double stranded RNAs of Fire et al., while longer than 21 base pairs, are not products of nature and would thus be recognized as "isolated" dsRNAs. After cleavage by Dicer, the resulting short RNAs would also be isolated dsRNAs regardless of where the cleavage by Dicer occurs and Fire et al. as evidenced by Zhang provides inherent anticipation of the instant claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within

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5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
July 31, 2006

83 TC 1600
JANE ZARA, PH.D.
PRIMARY EXAMINER